

CLAIMS

1. A process for rapid solution synthesis of a peptide in an organic solvent or a mixture of organic solvents, the process comprising repetitive cycles of steps (a)-(d):
  - 5 (a) a coupling step, using an excess of an activated carboxylic component to acylate an amino component,
  - (b) a quenching step in which a scavenger is used to remove residual activated carboxylic functions, wherein the scavenger may also be used for deprotection of the growing peptide,
  - (c) one or more aqueous extractions and
  - 10 optionally, (d) a separate deprotection step, followed by one or more aqueous extractions, characterised in that the process comprises at least one step (b), referred to as step (b'), in which an amine comprising a free anion or a latent anion is used as a scavenger of residual activated carboxylic functions.
- 15 2. The process of claim 1, wherein in step (a) the molar amounts of the reagents used are in decreasing order:  
carboxylic component, coupling additive > coupling reagent > amino component.
- 20 3. The process of claim 1, wherein in step (a) a pre-activated carboxylic component is used.
4. The process of any one of claims 1-3, wherein in step (b') an amine comprising a latent anion is used as the scavenger.
- 25 5. The process of claim 4, wherein the latent anion in the scavenging amine bears a temporary protecting group which can be selectively removed in the presence of any permanent protecting groups attached to the growing peptide.
- 30 6. The process of claims 4 or 5, wherein the latent anion in the scavenging amine bears a temporary protecting group which displays a lability similar to that of the temporary protecting group present at the N-terminus of the growing peptide.

7. The process of claims 5 or 6, wherein the temporary protecting groups are hydrogenolytically removable groups whereas the permanent protecting groups are acidolytically removable groups.
- 5 8. The process of claim 7, wherein the temporary protecting groups are of the benzyl type.
9. The process of any one of claims 4-8, wherein the scavenger is a primary amine comprising a free anion or a latent anion.
- 10 10. The process of claim 9, wherein the primary amine is a C-terminally protected amino acid derivative.
11. The process of claim 10, wherein the amino acid is  $\beta$ -alanine or a derivative thereof.
- 15 12. The process of claim 11, wherein the scavenger is benzyl  $\beta$ -alaninate or a salt thereof.
13. The process of any one of claims 1-8, wherein a thiol comprising a free or a latent anion is used as a scavenger instead of an amine comprising a free or a latent anion.
- 20 14. The process of any one of claims 1-13, wherein the process comprises one or more cycles wherein in step (b) a polyamine is used as the scavenger.
15. The process of any one of claims 1-14, comprising one or more cycles wherein in step (b) deprotection does not occur and the subsequent step (c) comprises sequential basic, acidic  
25 and basic extractions.
16. The process of claim 15, wherein the extractions are performed in the presence of sodium chloride or potassium nitrate.
- 30 17. The process of claim 15 or 16, comprising a subsequent step (d) which comprises deprotection and sequential basic and neutral extractions.

18. The process of claim 17, wherein the extractions are performed in the presence of sodium chloride or potassium nitrate.
19. The process of any one of claims 1-14, comprising one or more cycles wherein in step (b) both quenching and deprotection occur and the subsequent step (c) comprises sequential basic and neutral extractions.
20. The process of claim 19, wherein the extractions are performed in the presence of sodium chloride or potassium nitrate.
21. The process of any one of claims 1 - 20, wherein in the last cycle in step (a) the protecting groups of the carboxylic component display a similar lability to that of the permanent protecting groups of the growing peptide and in step (b) the scavenger is a polyamine.
22. The process of any one of claims 1-21, wherein the organic solvent or mixture of organic solvents is ethyl acetate or a mixture of ethyl acetate and dichloromethane, a mixture of ethyl acetate and 1-methyl-2-pyrrolidinone, a mixture of ethyl acetate and *N,N*-dimethylformamide or a mixture of ethyl acetate and tetrahydrofuran.
23. The process of any one of claims 1-22, wherein the process is performed within a temperature range of 0 to 50 °C.
24. The process of claim 23, wherein the process is performed at ambient temperature.
25. A method for combinatorial synthesis of peptide libraries using the split and mix method, wherein the process of any one of claims 1-24 is applied.
26. A method for automated solution synthesis of peptides, wherein the process of any one of claims 1-25 is applied.
27. A peptide or a mixture of peptides, prepared according to a process comprising the process of any one of claims 1-26.

